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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/693,028

Applicant(s)

HANNAH, ERIC C.

Examiner

Michael Borin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/23/2003</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Status of Claims

1. Claims pending are 1-13.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

A. Claim 1: The claim is vague and indefinite as neither the objective of the claim nor the steps resulting in the achieving the objective are clear. There is no preamble in the claim. The final step addresses "predicting tertiary structure". However, there are no method steps leading to "prediction". Contrary, the previous step addresses "refining" secondary structure based on already known and utilized set of topomers; no other method steps lead in the direction of "predicting tertiary structure". Neither the term "predicting tertiary structure", nor method steps leading to "predicting tertiary structure" are specified in claims or in specification.

B. Claim 1 is confusing in reciting steps "predicting", "superimposing" "refining" without specifying with particularity what methods steps are encompassed. The claim

does not provide sufficient information what is intended to be done and how or under what circumstances such steps would be made.

C. The term "smart moves" is vague and indefinite. The specification, although providing particular examples (e.g., Figure 2, paragraph [0014]), does not provide a standard how to predetermine the "smart moves", and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

Claim Rejections - 35 U.S.C. § 101/ 112-1

3. Claims 1-13 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific or substantial utility or a well established utility.

The instant claims are drawn to method comprising steps of predicting a secondary structure of a protein; superimposing the predicted secondary structure on a set of topomers; refining the superimposed secondary structure; and predicting a tertiary structure of a protein.

The Court of Customs and Patent Appeals has stated:

"Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public."

A “use” to do further research is not considered a utility which provides an “immediate benefit” to the public.

Examples of situations requiring further research to identify or reasonably confirm a “real world” context of use, and which do not have utility under 35 USC 101, as set forth in MPEP 2107.01.1, include:

- (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved',
and
- (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility.

The asserted utility of the instant method is predicting tertiary structure of a protein.

Orengo et al (Proteins:Structure, Functions, and Genetics. Suppl. 3:149-170, 1999) points out that :

“Predicting the 3-D structure of a protein without the assistance of structural data from evolutionary relatives or analogous protein folds is hardest category in CASP experiment”. Except in a small percentage of predictions, the final model was far too distant from the native structure ...”

See p. 149, last two paragraphs.

Further Russell (see full citation in the art rejection below) teaches that despite initially promising results, methods of fold recognition are not always accurate:

“Don't trust the alignments that are output by the programs. They can be used as a starting point, but the best alignment of sequence on to tertiary structure is still likely to come from careful human intervention.”

See <http://www.russell.embl-heidelberg.de/gtsp/foldrec.html>

The instant specification provides lists of method useful for carrying out intermediate steps of the method, but does not offer a single example of successful prediction of three dimensional structure of any single protein.

Thus, the instant method would require further research to determine whether the configurations determined thereby has any relevance to real world native structures.

The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter. Identifying use of the claimed design method would require carrying out further research. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In addition, there is no well established utility known for the method as claimed. Consequently, the claimed subject matter is not supported by substantial or well established utility.

4. Claims 1-13 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

In addition, even if the method had been enabled, the specification clearly teaches that that the method would be operable only if "superimposing" is not to a random set of topomers, but to set of topomers of structure that contain similar secondary structural elements in similar order [see paragaph [0063)]..

Claim Rejections - 35 U.S.C. § 101 (non-statutory invention)

5. Claims 1-22 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The rejection is based on recently released "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility"¹. The following analysis of facts of this particular patent application follows the analysis suggested in the "Guidelines". Note that the text of the Guidelines is italicized.

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.*
- The claimed invention otherwise produces a useful, concrete and tangible result, based on the factors discussed below.*

In the instant case, the claimed invention does not "transform" an article or physical object to a different state or thing. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

¹ Available at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/guidelines101_20051026.pdf

physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)

In the instant case, the question is thus whether the final result achieved by the claimed invention produces a result which satisfies all three criteria of being useful, and concrete, and tangible. In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, substantial, and credible. For a claim to be "tangible," the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be "concrete," the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself. In addition, a claim must be limited only to statutory embodiments. Thus, if the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

(1) "USEFUL RESULT" For an invention to be "useful" it must satisfy the utility requirement of section 101, i.e., it has to be (i) specific, (ii) substantial and (iii) credible.

When the examiner has reason to believe that the claim is not for a practical application that produces a useful result, the claim should be rejected, thus requiring the applicant to distinguish the claim from the three § 101 judicial exceptions to patentable subject matter by specifically reciting in the claim the practical application. In such cases, statements in the specification describing a practical application may not be sufficient to satisfy the requirements for section 101 with respect to the claimed invention. Guidelines, p. 21.

As discussed in the utility rejection above, the invention does not satisfy the criteria of utility requirements as not being specific and substantial.

*(2) "**TANGIBLE RESULT**" The tangible requirement require that the claim must recite more than a § 101 judicial exception, in that the process claim must set forth a practical application of that § 101 judicial exception to produce a real-world result. The opposite meaning of "tangible" is "abstract."*

A tangible requirement requires that the claim must set forth a practical application of the computational steps to produce a real-world result. No practical result is recited in the claims; thus the instant claims do not include any tangible result.

*(3) "**CONCRETE RESULT**" Usually, this question arises when a result cannot be assured. In other words, the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. The opposite of "concrete" is unrepeatable or unpredictable.*

In the instant case, the method seems to be concrete in that, for a given secondary structure it would "predict" a tertiary structure. However, as the set of topomers used to model secondary structure onto seems to be a random set of general

protein topologies (see paragraphs [0063]-[0064]) and the secondary structure seems to be determined based on a random choice of amino acid residues (see Fig.2), the result of such determining seems to be "is unrepeatable and unpredictable. Thus the result does not seem to be "concrete".

Thus, the final result achieved by the claimed invention produces a result which does not satisfy all three criteria of being useful, and concrete, and tangible.

Claim Rejections - 35 USC § 102 and 103

6. Claims 1-4,7,8 are rejected under 35 U.S.C. 102(b) as being anticipated by Monge et al. (Proc. Natl. Acad. Sci, 1994, 91, 5027-5029) or Freisner et al (US 5,600,571) or Russell et al ("A Guide to Structure Prediction", <http://www.russell.embl-heidelberg.de/gtsp/index.html>)

The instant claims are drawn to method comprising steps of predicting a secondary structure of a protein; superimposing the predicted secondary structure on a set of topomers; refining the superimposed secondary structure; and predicting a tertiary structure of a protein.

Topomers are general protein folds (conformations, candidate structures) for a protein of a given length. "Superimposing" the structure on a set of topomers is modeling of the combination of secondary structure elements on a set of said general protein candidate structures. See specification., paragraphs [0063], [0064].

Monge teaches a method of predicting tertiary structure of a protein by modeling its secondary structure (p. 5027, right column, second full paragraph), modeling on

possible candidate structure, evaluating its compactness and energy level (p. 5027, right column, third full paragraph), refining secondary structure, (e.g., by Monte Carlo or simulated annealing methods) and identifying tertiary structure again (p. 5027, last paragraph).

Freisner et al. (US 5,600,571) teaches method of predicting three dimensional structure of a protein. Freisner teaches that one method of approaching predicting three dimensional structure is to fix the protein secondary structure. From an energetic viewpoint, one can imagine decomposing the potential function into helix to β -sheet stabilization terms and the remaining terms representing long range hydrophobic, electrostatic, and van der Waals interactions. In the case of proteins, there is a natural segmentation of the polymer chain into well-defined secondary structural units (i.e. helices to loops). In particular, α -proteins are considered which consist of relatively rigid helices connected by flexible loop regions. By constructing a model based on these structural units rather than the individual amino acids, the number of independent polymer segments is reduced by roughly an order of magnitude. See columns 1-2. The method of Freisner first generates a simple model in which residues are described by a discrete set of ϕ - ψ dihedral angle conformations. The method further applies an algorithm which makes use of the assigned secondary structure to construct a representation of the molecule where helices and loops are described by cylinders and spheres respectively. Correspondence with the residue conformations is maintained by using loop geometries from a list of structures calculated using the allowed dihedral angles in segments of the appropriate length (i.e., superimposing to set of topomers). Further optimization then consists of a Monte Carlo simulated annealing procedure combined with a genetic algorithm in which additional structures are generated by

combining different members of the ensemble. See col. 4, first and last full paragraphs, and claims 1-8.

Russell offers "A Guide to Structure Prediction" of proteins (See <http://www.russell.embl-heidelberg.de/gtsp/index.html>; version 2.0 is released 09/1999 and is reiteration of the original lecture presented for British Biophysical Society Meeting in 1996²). The guide summarizes methods leading to predicting three dimensional structure of a protein which include generation secondary structure, preferably a consensus secondary structure (see <http://www.russell.embl-heidelberg.de/gtsp/secstrucpred.html>)³, modeling secondary structure on possible candidate structures and refining the secondary structure (<http://www.russell.embl-heidelberg.de/gtsp/famanal.html>). Thus, for glutamyl tRNA reductase predicted secondary structure was aligned to the core elements, refined (several alpha helices and beta strands from predicted secondary structure were deleted) to allow for alignment (see <http://www.russell.embl-heidelberg.de/gtsp/famanal.html>)

7. Claims 2-13 are rejected under 35 U.S.C. 103(a) as unpatentable over Monge et al. or Freisner et al , or Russell et al and further in view of Evans et al (Protein Science, 1995, 4, 1203-1216) and Andricioaei (Journal of Chemical Physics, 04/2001, Vol.114 (16), pp. 6994-7000) or Zhou et al (The Journal of Chemical Physics, 1997,

² see <http://www.cbi.pku.edu.cn/docbak/homo-model-course/flow.html>

³ references are provided as links to particular slides of Russel's presentation; the printout of the preface and cited slides is also attached.

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107,9185-91960), and Debe et al. (Proc. Natl Acad Sci, 1999, 96,2596-2601) and Sadanobu et al. (J. Chem. Phys. 106:6722, 1997)

In regard to dependent claims, if there are any differences between Applicant's claimed methods and that of the prior art, the differences would be appear minor in nature. The methods used at particular steps of the instant invention are well known in the art and their use would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made. For example, methods and software packages for secondary structure prediction and refinement are described in Freisner et al, Russell, and further in Evans et al.; methods for various ways of applying Monte Carlo method are addressed in Freisner et al, as well in Andricioaei et al or Zhou et al., determining topomers and use of Continuous Configuration Boltzman Biased Direct Monte Carlo Method to determine topomers is described in Debe et al and Sadanobu et al., respectively, a variety of programs is known to construct and refine protein secondary structure , such as AMBER, CHARMM, X-PLOR, INSIGHTII, was available at the time of filing; etc.

Conclusion.

8. No claims are allowed

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb
06/03/2006